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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/788,552	02/21/2001	Serge Braam	032751-053	5627

7590 02/20/2003

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EXAMINER
SHUKLA, RAM R

ART UNIT	PAPER NUMBER
2632	17

DATE MAILED: 02/20/2003

Please find below and or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

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Application No.	Applicant(s)
09/788,552	BRAUN, SERGE
Examiner	**Art Unit**
Ram R. Shukla	1632

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 December 2002*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24,25,33-35 and 43-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24,25,33-35 and 43-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1 ☐ Certified copies of the priority documents have been received.

2 ☐ Certified copies of the priority documents have been received in Application No. _____.

3 ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). ___
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Amendments and response filed 12-11-02 have been received and entered.

2. Objection to the specification for lacking the priority data in the first sentence is withdrawn in view of the applicants' arguments.

5. Claim 24, 25, 33-35 and 43-45 are pending.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 24, 25, 33-35 and 43-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating multiple sclerosis, wherein a nucleic acid encoding beta-interferon comprising beta-interferon secretory signal is directly administered to muscle cells and a pharmaceutical composition comprising an effective amount of a nucleic acid encoding beta-interferon comprising beta-interferon secretory signal, wherein the composition is nucleic acid is DNA or naked DNA, wherein the DNA is associated with a transfection-facilitating vehicle and wherein the transfection facilitating vehicle is selected from a list of cationic lipids, cationic polymers and polypeptides and wherein the pharmaceutical composition is suitable for injection, does not reasonably provide enablement for a method of treating any immune disease or any demyelinating disease or wherein the nucleic acid is administered by any route and other embodiments for reasons of record set forth in the previous office action of 1-15-02 and 8-12-02. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Response to Arguments

Applicant's arguments filed 5-15-02 have been fully considered but they are not persuasive. It is noted that applicants amended claims 24 and 25 by reciting multiple sclerosis in place of an immune disease and naked DNA in place of a nucleic acid. While these amendments addressed the issue of treating any immune disease, the amendment does not address other issues, for example any method of administration (see the office action of 8-12-02).

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 45 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 45 recites the limitation "said nucleic acid" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 25 and 34-35 rejected under 35 U.S.C. 102(b) as being anticipated by Croxford et al (The Journal of Immunology 160:5181-5187, 1998).

This art teaches a vector for expression of interferon beta in mice model of EAE, which are accepted models for MS (see the methods section on page 5182, left and right columns, results section on page 5182 right column to left column on

5185 and the discussion section). The IFN protein is secreted in culture supernatant, therefore it has a secretory signal.

Accordingly, this art anticipates the claimed invention of claims 25 and 34-35.

12. Claims 25 and 34-35 rejected under 35 U.S.C. 102(b) as being anticipated by Triantaphyllopous et al (Arthritis & Reumatism 42:90-99, 1999).

This art teaches a vector for expression of interferon beta and a method for introducing the vector in mice model of EAE (see the methods section on page 91, results section on page 93-96 and figure 4). The IFN protein is secreted in culture supernatant, therefore it has a secretory signal.

Accordingly, this art anticipates the claimed invention of claims 25 and 34-35.

13. Claims 25 and 34-35 are rejected under 35 U.S.C. 102(B) as being anticipated by Triantaphyllopous et al (Gene Therapy 5:253-263, 1998).

This art teaches a vector for expression of interferon beta and a method for introducing the vector in mice model of EAE (see the methods section on page 259, left and right columns, results section on page 257, left column and discussion). The IFN protein is secreted in culture supernatant, therefore it has a secretory signal

Accordingly, this art anticipates the claimed invention of claims 25 and 34-35.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 24, 25, 33-35 and 43-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Triantaphyllopous et al (Gene Therapy 5:253-263, 1998) in view of Youssef et al (The Journal of Immunology 161:3870-3879, 1998) and Felgner et al (US Patent 5,580,859, 12-3-1996).

At the time of the invention, Triantaphyllopous et al taught a vector for expression of interferon beta and a method for introducing the vector in mice model of EAE (see the methods section on page 259, left and right columns, results section on page 257, left column and discussion). The art also taught that IFN-beta had a beneficial effect on the disease course in relapsing-remitting multiple-sclerosis (MS) patients, shown by reductions in both the magnetic resonance imaging lesions and the severity and frequency of relapse (see the second paragraph of introduction in column 1 continued in column 2). The art also taught intracranial injection of IFN beta vector to mice before the onset of EAE and that the LTR driven IFN beta was more efficient in blocking disease severity compared to NSE promoter driven INFN beta. The art also teaches that feasibility of expressing IFN-beta by gene therapy in animal models of human disease will help to clarify its role in pathogenesis and its mechanism of action in therapeutic interventions of autoimmune diseases, cancer etc (see the discussion on page 257, right column).This art does not teach treatment of MS by administering a naked DNA expressing beta-interferon in a patient.

Youssef et al teaches a DNA vaccination with chemokines for treating EAE (see the abstract and the methods section). They further teach the novelty of DNA vaccination in expressing foreign antigens as well as for expressing cytokines (see the discussion in the second column on page 3877).

At the time of the invention, it was routine in the art to directly administer naked DNA molecules to tissues for providing a therapeutic protein for treating diseases and for vaccination (see Felgner et al).

At the time of the invention, it would have been obvious to an artisan of ordinary skill in the art to directly inject a naked DNA vector expressing IFN-beta to a MS patient with a reasonable expectation of success. An artisan would have been motivated to treat MS by directly injecting naked DNA encoding IFN-beta because direct DNA injection is simple and naked DNA was known to work for expressing other proteins related to MS development. Regarding claims 33 and 43, it is noted that it would have been obvious to use human sequences when treating a patient to minimizing the effects of any differences between mouse and human sequences and the sequences encoding human IFN-beta were known in the art or an artisan of skill would have had isolated it with a reasonable expectation of success.

16. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will

the statutory period for reply expire later than SIX MONTHS from the date of this final action.

When amending claims, applicants are advised to submit a clean version of each amended claim (without underlining and bracketing) according to § 1.121(c). For instructions, Applicants are referred to http://www.uspto.gov/web/offices/dcom/olia/aipa/index.htm.

Applicants are also requested to submit a copy of all the pending/under consideration claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for this Group is (703) 308-4242. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the William Phillips whose telephone number is (703) 305-3413.

RAM R. SHUKLA, PH.D
PATENT EXAMINER

Ram R. Shukla, Ph.D.
Primary Examiner
Art Unit 1632